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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/664,513	09/16/2003	Marc K. Hellerstein	416272003700	4651
20872	7590	03/30/2006	EXAMINER	
MORRISON & FOERSTER LLP 425 MARKET STREET SAN FRANCISCO, CA 94105-2482			MARTIN, PAUL C	
			ART UNIT	PAPER NUMBER
			1655	
DATE MAILED: 03/30/2006				

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/664,513	HELLERSTEIN, MARC K.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Paul C. Martin	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 21 February 2006.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-29 is/are pending in the application.
- 4a) Of the above claim(s) 4-7, 9-20, 27-29 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-3, 8, 21-26 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

All objections and rejections not repeated in the instant Action have been withdrawn due to Applicant's response to the previous Action.

### ***Double Patenting***

This rejection is maintained for reasons of record set for in the paper mailed 10/20/05, repeated below:

Claims 1, 2, 8, 21, 23, 24 and 26 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 4-6 and 11 of U.S. Patent No. 6,010,846. Although the conflicting claims are not identical, they are not patentably distinct from each other because although the conflicting claims are not identical, they are not patentably distinct from each other because the claims 1-2, 8, 21, 23, 24 and 26 are "anticipated" by claims 1, 4-6, and 11 of U.S. Patent No. 6,010,846 because the scope of the claims 1-2, 8, 21, 23, 24 and 26 falls entirely within the scope of claims 1, 4-6, and 11 of U.S. Patent No. 6,010,846.

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Claims 1-3, 8, and 21-26 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 5-8, 13, 26, 29 and 31 of copending Application No. 10/701,990. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-3 and 8 are "anticipated" by claims 27 and 31 of Application No. 10/701,990 and claims 22-26 are made obvious by claims 27 and 31.

Although claims 27 and 31 of 10/701,990 does not specifically teach the particulars of instant claims 22-26, i.e., wherein the isotopically labeled precursor molecule is administered orally or wherein the living system is an animal, mammal, rodent or human, the ordinary artisan would have been motivated to administer the labeled precursor molecule orally to an animal, mammal, rodent, or human in order to assess the metabolic processing of the isotopically labeled precursor molecule. It is clear from claim 1 of 10/701,990 that the labeled sugars administered to an "individual", which is the genus of humans or rodents for example, thereby making obvious the species of humans and rodents.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant's arguments have been fully considered but they are not deemed persuasive. Applicant maintains that the rejection does not make clear the differences between the inventions defined in the conflicting claims and reasons why a person of ordinary skill in the art would conclude that the invention defined in the rejected claims are obvious variants of the patented claims. Applicant argues that the '846 patent does not teach a method for assessing metabolic fitness of aerobic demand of a living system. In response to applicant's arguments, the recitation has not been given patentable weight because the recitation occurs in the preamble.

### ***Response to Argument***

A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951). The cited claims of '846 are directed toward a method for measuring a rate of cellular proliferation or cellular destruction, such rate being an indicator of the overall metabolic fitness of a living system. Cellular proliferation and/or destruction is directly linked to the increase and/or decrease in the intake and turnover of nutrients and waste products (metabolism) and a measure of one will necessarily give a value for the other.

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Applicant argues that the '846 patent does not disclose a "mitochondrial molecule" and that the patent is directed toward total cellular DNA, not mitochondrial DNA. Applicant acknowledges that DNA is found in mitochondrial cells and therefore the claimed invention falls within the scope of the patent as DNA is a mitochondrial molecule. It would have been obvious to one of ordinary skill in the art that an assessment of cellular DNA would necessarily encompass genomic and mitochondrial DNA, and any isotopically labeled precursor molecule would be a precursor for both genomic and mitochondrial DNA. Moreover, though it is acknowledged that the claims are not identical, the scope of the claims 1,2,8, 21, 23, 24 and 26 of Application # 10/664,513 is entirely within the scope of the claims 1, 4-6, and 11 Patent 6, 010, 846.

Similarly, Claims 1,2, 5-8, 13, 26, 27, 29, and 31 of Application 10/701,990 are anticipatory of Claims 1-3, 8, and 21-26 of Application 10/664,513. Applicant argues that the method of 10/701,990 to determine metabolism in an individual is not equivalent to assessing the metabolic fitness or aerobic demand of a living system. In response to applicant's arguments, the recitation has not been given patentable weight because the recitation occurs in the preamble.

***Response to Arguments***

A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951). Claim 1 of 10/701,990 teaches a method for determining the metabolism of an isotopically labeled precursor molecule able to be utilized by mitochondrion, and detecting incorporation (into cellular DNA including mitochondrial DNA, as well as other cellular products) and determining the metabolism (biosynthesis and breakdown) of the isotope into water, said water being a byproduct of cellular metabolism. A determination of metabolism will necessarily give one of ordinary skill in the art a view of the metabolic fitness of a living system, for example if no isotope labeled water is detected the living system is not processing the precursor molecule as would normally be expected in a healthy system. Applicant argues that the total oxidative metabolism is broader in scope than "metabolism" in that it involves fuels beyond sugars and fatty acids, and simultaneously narrower than the metabolism of sugars and fatty acids.

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The Examiner is unsure of the intended meaning of the paradox presented and maintains that one of ordinary skill in the art at the time of the instant invention would have understood that the administration of an isotopically labeled sugar or fatty acid (precursor molecule) to an individual (living system), said isotope being incorporated (via metabolism into total DNA, both genomic and mitochondrial) and detecting the isotopic content of the isotope into a final cellular byproduct to determine the metabolism (biosynthesis and breakdown) of the precursor molecule as taught by Claim 1 of Application 10/701,990 anticipates the administration of an isotopically labeled precursor molecule to a living system for a time sufficient for incorporation of the isotopically labeled molecule into a mitochondrial molecule (DNA), and measuring the isotopic pattern (gain/loss) of the mitochondrial molecule, and calculating the rate of synthesis or degradation of the mitochondrial molecule (determined by isotope in water byproduct) to assess metabolic fitness (metabolism).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.



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A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

***Claim Rejections - 35 USC § 102***

Claims 1-3, 8, and 21-26 are rejected under 35 U.S.C. 102(b) as being anticipated by Hellerstein (5,910,403).

This rejection is maintained for reasons of record set forth in the paper mailed 10/20/05, repeated below:

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Hellerstein teaches a method of administering the isotopically labeled precursor molecule  $H^2$ -labeled glucose to both animal (Rat) and human subjects for a time sufficient for the label to be incorporated into deoxyribonucleic acid in the subject, (Column 10, Lines 46-67 and Column 11, Lines 1-27), measuring the isotopic content, pattern, rate of change of isotopic content or pattern of the deoxyribonucleic acid (Column 10, Lines 65-67 and Column 11, Lines 20-22), and calculating the rate of synthesis of deoxyribonucleic acid in the subject (Table 3 and Column 16, Lines 6-7 & Fig.8)

Hellerstein teaches the step of measuring the isotopic content, pattern, rate of change of isotopic content or pattern of the deoxyribonucleic acid by Gas Chromatograph Mass Spectrometry. (Column 10, Line 67 & Fig.2 and Column 11, Line 21).

Hellerstein teaches the method wherein the isotopically labeled precursor molecule is administered orally. (Column 9, Line 36).

Claims 1, 2, 8, 21, 23, 24 and 26 are rejected under 35 U.S.C. 102(b) as being anticipated by Hellerstein. (6,010,846)

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Hellerstein teaches a method of administering an isotopically labeled precursor molecule to human (animal, mammal) subjects with a detectable amount of the label to be incorporated into deoxyribonucleic acid in the subject, (Column 28, Lines 20-35; Column 25, Lines 6-16), measuring the isotopic content, pattern, rate of change of isotopic content or pattern of the deoxyribonucleic acid (Column 24, Lines 59-67; Column 25, Lines 1-2 and Fig.2 and Column 25, Lines 24-26), and calculating the rate of synthesis of deoxyribonucleic acid in the subject (Table 2, Column 29, Lines 34-47 and Fig. 7).

Hellerstein teaches the step of measuring the isotopic content, pattern, rate of change of isotopic content or pattern of the deoxyribonucleic acid by Gas Chromatograph Mass Spectrometry. (Column 25, Lines 1-2, 24-25 and Fig. 2 ).

### ***Response to Arguments***

Applicant argues 5,910,403 does not teach a method for assessing metabolic fitness or aerobic demand of a living system through the detection of isotope label incorporation into a mitochondrial molecule and that a measurement of cellular proliferation via DNA synthesis rate does not provide an assessment of metabolic fitness or aerobic demand.

The Applicant's arguments are not found persuasive for the following reasons, that 5,910,403 teaches the use of cellular proliferation and destruction rates as a means for assessing response to exercise training or physical therapy in myocytes or mitochondria in myocytes (Column 9, Lines 11-13), administration of an isotopically labeled precursor molecule to a living system for a time sufficient for the labeled precursor to be incorporated into a mitochondrial molecule (DNA is a known mitochondrial molecule), measuring the isotopic content, pattern, rate of change of isotopic content or rate of change of an isotope label incorporation into a mitochondrial molecule (DNA is a known mitochondrial molecule), and calculating the rate of synthesis of the mitochondrial molecule (DNA) to assess the metabolic fitness of the living system.

Applicant argues that 6,010,846 does not teach a method for assessing metabolic fitness or aerobic demand of a living system through the detection of isotope label incorporation into a mitochondrial molecule and does not teach the specific use of "mitochondrial molecules" and that the patent does not teach the use of mitochondrial DNA.

The Applicant's arguments are not found persuasive for the following reasons, 6,010,846 teaches the use of cellular proliferation and destruction rates as a means for assessing response to exercise training or physical therapy in myocytes or mitochondria in myocytes (Column 15, Lines 25-27), administration of an isotopically labeled precursor molecule to a living system for a time sufficient for the labeled precursor to be incorporated into a mitochondrial molecule (DNA is a known mitochondrial molecule), measuring the isotopic content, pattern, rate of change of isotopic content or rate of change of an isotope label incorporation into a mitochondrial molecule (DNA is a known mitochondrial molecule), and calculating the rate of synthesis of the mitochondrial molecule (DNA) to assess the metabolic fitness of the living system. Applicant asserts that the patent does not teach the use of mitochondrial DNA, however the claimed invention merely teaches a mitochondrial molecule which is DNA used in the method, while 6,010,846 inherently discloses mitochondrial DNA as a function of the measurement of total cellular DNA of which mitochondrial DNA is a part of.

***Conclusion***

**No Claims are allowed.**

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul C. Martin whose telephone number is 571-272-3348. The examiner can normally be reached on M-F 8am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on 571-272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Paul Martin  
Examiner  
Art Unit 1655

03/17/06

RICIA LEITH  
...MARY EXAMINER  
